AMENDMENTS TO THE SPECIFICATION

Please amend the Title as follows:

High Contrast Optoacoustic ~~Optoacoustical~~ Imaging Using Nanoparticles

Please amend the paragraph beginning on page 2, line 1 as follows:

The term "optoacoustic imaging" as used herein applies to any imaging method in which electromagnetic radiation generates a detectable pressure wave or sound from which an image is calculated. Optoacoustic imaging is equivalent in meaning to the term, "photoacoustic imaging," used by others to refer to the same technology. However, the term "optoacoustic" is not universally so used, and indeed has been combined with the word "imaging" by Unger and Wu in U.S. Pat. No. 6,123,923 to describe a different imaging technology (light irradiation of their method plays no role in the generation of a detected acoustic signal). As used herein, the term "optoacoustic imaging" as used by Unger and Wu in U.S. Pat. No. 6,123,923 has no relevance to light irradiated optoacoustic ~~optoacoustical~~ imaging.

Please amend the paragraph beginning on page 3, line 24 as follows:

There would be real benefit in having a light based detection system that can detect objects as small as 1 mm. Imaging resolution on the order of 1 mm is necessary for tumor detection at a stage when it is readily treatable. The general wisdom is that smaller size tumors will be easier to cure. There is a significant medical need for imaging methods that boost both sensitivity and resolution to about 1 mm or smaller. Greater sensitivity will allow the detection of both smaller tumors and tumors that have reduced blood content because they are in an early stage of development or because of therapeutic interventions. Tumors in the prostate or breast or in other organs at such an early stage of development may be termed "nascent tumors." Nascent tumors differ from precancerous lesions in they contain identifiable cancerous cells. However, they have not yet developed into recognizable tumor masses. In particular, they have not yet developed the extensive vascular network that is characteristic of many larger solid tumors. For detection of nascent cancerous tumors, it may no longer be sufficient to rely on differences in the blood content and normal tissue. The blood content of a nascent cancerous tumor is likely to be similar to that of normal tissue. An alternative detection strategy will be required. Currently, however, neither pure optical imaging can nor prior optoacoustic ~~optoacoustical~~ imaging could detect tumors as small as 1 mm. It is unlikely that images of the interior of the human breast or any other thick part of the body will ever be produced by pure optical imaging with a resolution of about 1 mm.

Please amend the paragraph beginning on page 4, line 8 as follows:

Other than detection of cancers, near infrared optoacoustic ~~optoacoustical~~ imaging has important other advantages, as will be further detailed below in describing various embodiments of our invention.

Please amend the paragraph beginning on page 4, line 16 as follows:

We have now discovered a way in which to optoacoustically detect the presence of objects as small as 1 mm and smaller in a body which can be penetrated by electromagnetic radiation. We have discovered that at least partially metallic nanoparticulates fabricated or manipulated to be non-spherical not only will shift the optical absorption spectrum into the near infrared range for deeper penetration into a body but also will both narrow the absorption band and simultaneously increase the effective absorbance, in certain instances by about an order of magnitude or more, thereby greatly increasing the optoacoustic efficacy of the nanoparticulate, making the manipulated nanoparticulate a very high contrast optoacoustic imaging agent. In accordance with our discoveries, effective acoustical response to electromagnetic radiation is increased by tailoring the choice of the composition, non-spherical shape and size of nanoparticulates to maximize both the optical absorbance of the particles at the irradiation wavelength(s) and the optoacoustic ~~optoacoustocal~~ pressure produced in response to absorbed electromagnetic energy.

Please amend the paragraph beginning on page 5, line 4 as follows:

In accordance with the invention, electromagnetic radiation is directed onto the body. The electromagnetic radiation has a specific wavelength or spectrum of wavelengths in the range from ~~300~~ 3 nm to 300 mm selected so that the wavelength or wavelength spectrum is longer by a factor of at least 3 than the minimum characteristic dimension of the nanoparticulate. The nanoparticulate absorbs the electromagnetic radiation more than would one or more non-aggregated spherically shaped particles of the same total volume with a composition identical to the nanoparticulate. The nanoparticulate by such absorption produces an enhanced optoacoustic signal resulting from the absorption. The optoacoustic signal can then be received and converted into an electronic signal characterized by at least one parameter selected from amplitude, frequency, phase, temporal profile, time of arrival, frequency spectrum, or a combination of any one or more of such parameters. The electronic signal may then be presented for assessment of the at least one parameter by a human or a machine.

Please amend the paragraph beginning on page 14, line 23 as follows:

The selected wavelength or selected spread of wavelengths of electromagnetic radiation used in connection with at least partially metallic nanoparticles of formed shape for this invention is selected from

the spectrum of wavelengths in the range from 3 ~~300~~ nanometers to 300 millimeters. In an embodiment the wavelengths are in the visible and near infrared spectrum. Suitably the spectrum is in the wavelength range from 650 nanometers to 1150 nanometers. Advantageously, the nanoparticles comprise gold and the wavelength for irradiation is from about 520 nanometers to about 1120 nanometers.

Please amend the paragraph beginning on page 44, line 16 as follows:

The practice of the present invention is not limited to the methods of U.S. Pat. No. 5,840,023 and encompasses the acquisition of an optoacoustic image with the aid of contrast agents comprising non-spherical at least partially metallic nanoparticulates, which may comprise a single metal or may be composites of different metals or may be filled metal shells, tuned to the wavelength of the irradiation, which may be anywhere in the electromagnetic spectrum from about ~~300~~ 3 nm to about 300 mm. However, wavelengths in the visible or infrared range from about 450 nm to about 1500 nm are preferred. More preferred is irradiation in the near-infrared wavelength range from 650 to 1200 nm. The irradiation can be generated with a laser, but the invention encompasses the use of any radiation source, regardless of whether it can be called a laser or not.